

Minocycline-Induced Hyperpigmentation: Treatment With the Q-Switched Nd:YAG Laser

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Background and Objective: Cutaneous hyperpigmentations are well-documented, but nevertheless rare side-effects of high-dose or long-term minocycline therapy. The pigmental changes, may last for years, even though therapy has been abrogated. To date, no safe and effective therapy has been described to target this cosmetically disturbing sequela.

Study Design/Materials and Methods: A 57-year-old female patient with extensive pigmental changes of the face due to long-term minocycline therapy was treated in eight consecutive sessions with the Q-switched Nd:YAG-laser (1,064-nm wavelength, 5- to 7-nsec impulse length).

Results: A 90% resolution of the pigmentation could be achieved after five treatments. After the last session the lesions were completely gone; no hypopigmentation scars, or other side-effects were observed.

Conclusion: Treatment with the Q-switched Nd:YAG laser seems to be an effective, safe, and easily applicable strategy for the therapy of minocycline-induced hyperpigmentations. *Lasers Surg. Med.* 22:223–227, 1998. © 1998 Wiley-Liss, Inc.

Key words: Nd:YAG laser; minocycline; hyperpigmentation

INTRODUCTION

Minocycline is a semisynthetic tetracycline which possesses a wide range of antimicrobial activity. Long-term and/or high-dose therapy may lead to cutaneous hyperpigmentations, which could persist over years, despite abrogation of treatment [1–3]. While iron- and melanin-containing granula in dermal macrophages seem to play a pivotal role, the exact mechanism of minocycline-induced pigmental changes is not yet completely understood. Until recently, no effective therapeutic measures to target this disorder have been described. Last year, however, three different groups independently reported on the treatment of minocycline-induced hyperpigmentations with the Q-switched ruby laser [4–6]. In the present case, we used the Q-switched Neodymium (Nd):YAG laser (1,064-nm wavelength, 5- to 7-nanosec impulse), which has been effectively applied in the removal of professional and

traumatic tattoos [7–9]. Our female patient had experienced facial hyperpigmentations, which showed up during long-term minocycline treatment of acne vulgaris. The pigmental changes lasted even after the antibiotic was discontinued. Eight treatments with the Nd:YAG laser led to a complete removal of the periorbital hyperpigmentations.

PATIENT AND METHODS

In June 1996, a 57-year-old female patient came to our clinic, suffering from dark, black-grey, periorbital and temporal facial hyperpigmentations (Figs. 1 and 2). The pigmental changes had appeared with increasing intensity

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Fig. 1. A 57-year-old female patient with periorbital and temporal minocycline-induced hyperpigmentations (front view).

since 1993. Between 1992 and 1995, the patient had been treated for acne vulgaris with 100 mg minocycline daily. The dose was reduced to 50 mg/day, beginning in June 1995; in November 1995, the medication was discontinued. Unfortunately, the hyperpigmentations did not disappear after cessation of the treatment and seemed to be unaltered at the beginning of the treatment (June 1996). We treated the patient in 1-month intervals using the Q-switched Nd:YAG laser. A 1,064-nm Nd:YAG laser was used (Medlite, Continuum Biomedical Inc., Santa Clara, CA) with an impulse duration of 5–7 nsec. The applied energy fluence lay between 5.3 and 6.7 J/cm². Local anesthesia was not required; we instructed the patient not to manipulate on the delicate crusts and to avoid sun exposure for at least 6 weeks.

RESULTS

A 90% resolution of the pigmentation could be achieved already after five treatments. Three more sessions were carried out to target the minimal residual changes at the lateral corner of the left eye (Figs. 3 and 4). The laser treatment showed no side effects, especially hypopigmentations or scars could not be detected.

DISCUSSION

Both the Q-switched Nd:YAG laser (1,064 nm and 532 nm, respectively) and the Q-switched ruby laser (694 nm, 10 and 40 nsec, respectively) have led to good-to-excellent results in the treatment of professional and traumatic tattoos [7–12]. The mechanism of action of both appliances is the selective photothermolysis of pigmented dermal cells [13–15]. The laser light is absorbed by pigmented structures, e.g., melanosomes or exogenously induced colored pigments, and transformed into thermal energy. As a consequence, melanosomes rupture, which leads in turn to the lysis of melanosome-containing cells, induced by photo-acoustic “shock waves” [7]. Tattoo-pigments or dirt-sprinkles in traumatic tattoos are blown into smaller particles by the absorbed thermal energy and are subsequently removed by phagocytic cells. A small portion of pigments is eliminated transdermally by crusting [10,16]. As the impulse duration of the Q-switched lasers is well under the thermal relaxation time of the cells, diffusion of heat into the surrounding tissue is negligible. Therefore, neighboring structures are only minimally affected, and scarring or hyper- and hypopigmentations are rarely ob-



Fig. 2. Same patient as in Figure 1, side view. The pigmental changes appear as patchy, greyish lesions.

served. If post-therapeutic pigmental changes occur, they are always transient and resolve within 6 months [7–12,14,16].

The Q-switched Nd:YAG laser penetrates deeper into the dermis and is less absorbed by melanin than the ruby laser. This is due to its longer wavelength (1,064 vs. 694 nm). In two studies, a lower rate of side-effects in the treatment of tattoos was described for the Nd:YAG-laser when compared to the ruby laser [7,8]. The Q-switched Nd:YAG laser is especially suited for the removal of brown-black, black-blue, and red tattoos, the latter when applied in the frequency-doubled mode (532 nm) [7,8,10–12].

Minocycline-induced hyperpigmentations can be classed into two groups: Type I are blue-grey pigmentations of inflamed or scarred skin, or of normal skin with preferential appearance on the legs and on the face [1,3,5,6,17–21]. Type II shows blue-brown pigmentations on the whole body, which are aggravated on sun-exposed areas [2,18,22]. Histologically, type I is characterized by a high number of pigment-loaded dermal macrophages and positive signals in the iron- and Fontana-Masson staining for melanin [1,17,20,21]. The more generalized type II hyperpigmentations are localized around the epidermal basement

membrane [18,22]. The exact mechanism of minocycline-induced pigmental changes is not completely understood. It has been suggested that minocycline and its derivatives act as iron-chelators and form complexes, which, when large enough, show as pigments [3]. Furthermore, minocycline, which is a yellow, crystalline substance, turns black when oxidized [2]. Dermal, pigment-loaded macrophages in type I minocycline-induced hyperpigmentations are an ideal target for the Q-switched Nd:YAG laser. In our patient, pigmentation of the lateral periorbital area could be abrogated completely by eight treatments. Scars, or transient hyper- or hypopigmentations did not occur. Failure of Nd:YAG treatment, which has been described by Tsao et al. [6], can be attributed to two circumstances: First, a considerably lower fluence was used (5.0 J/cm^2 vs. a maximum of 6.7 J/cm^2 in our case), and second, only a small area ($1 \times 1 \text{ cm}$) was treated experimentally and only once. Type II minocycline-induced hyperpigmentations may not be treated effectively with the Q-switched Nd:YAG-laser, as the 1,064-nm laser light is absorbed by the epidermal melanin only to a small percentage. For this entity, the Q-switched ruby laser might be the adequate treatment option.



Figs. 3 and 4. Clinical situation of the patient after eight treatments with the Nd:YAG-laser. The lesions have disappeared completely. No scarring or hypopigmentations can be detected.

In summary, both Q-switched laser systems, the Nd:YAG laser as well as the ruby laser, have been proven as effective, safe, and elegant devices for the treatment of minocycline-induced hyperpigmentations. Due to the low rate of side-effects, even delicate and cosmetically relevant facial areas as the periorbital region can be targeted unproblematically.

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